

**ATTORNEY'S DOCKET NUMBER: 2008725-0051**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Stock *et al.* Examiner: Gitomer, Ralph J.  
Serial Number: 10/579,369 Art Unit: 1657  
Filed: May 15, 2006 Conf. No.: 3055  
For: METHOD OF IDENTIFYING MODULATORS OF PP2A MEHYLASE

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**TRANSMITTAL**

Applicant filed an Information Disclosure Statement (IDS) on April 6, 2010, and indicated that copies of (1) one English language translation of a Japanese patent application and (2) several non-patent literature references were not included in the IDS submission. All such references were marked with a dagger (†) on the PTO Form SB/08. In the IDS submission, Applicant included a statement that copies of these references would be forthcoming.

Between submission of the IDS on April 6, 2010, and the present date, May 28, 2010, the Examiner issued a Notice of Allowance on April 26, 2010, and indicated that all of the references listed on the PTO Form SB/08 submitted on April 6, 2010, including the references marked with a dagger, had already been considered by the Examiner. For purposes of completeness, however, Applicant submits herewith copies of all of the daggered references, which are as follows:

B22†	JP-2000037188-A	02-08-2000	Max Planck Gesellschaft
C2†	ACKER et al., "Photometric determination of shell constituents in cocoa products," 1966, Suesswaren (Hamburg), 15(10):622-4, 626-8		
C19†	BLICKENSTAFF et al., "Potential radioprotective agents-V. Melatonin analogs. Oral activity of p-aminopropiophenone and its ethylene ketal," 1994, <i>Bioorganic &amp; Medicinal Chemistry</i> 2(10):1057-60		
C20†	BLICKENSTAFF et al., "Potential radioprotective agents. 1. Homologs of melatonin," 1994, <i>J. of Pharmaceutical Sciences</i> , 83(2):216-18		
C25†	BRAMBLETT, et al, "Abnormal Tau Phosphorylation at Ser396 in alzheimer's Disease Receptitulates Development and Contributes to Reduced Microtubule Binding," 1993, <i>Neuron</i> , 10:1089-1099.		
C28†	BRYANT et al., "Methylated C-terminal Leucine Residue of PP2A Catalytic Subunit is Important for Binding of Regulatory B Subunit," 1999, <i>Biochemical Journal</i> , 339(2):241-246, ISSN: 0264-6021		
C30†	Buée et al., "Tau protein isoforms, phosphorylation and role in neurodegenerative disorders," 2000, <i>Brain Res. Rev.</i> , 33(1):95-130		
C31†	CAUDILL et al., "Intracellular S-Adenosylhomocysteine Concentrations Predict Goba DNA		

	Hypomethylation in Tissues of Methyl-Deficient Cystathionine $\beta$ -Synthase Heterozygous Mice," 2001, American Society for Nutritional Sciences, 131:2811-2818.
C33†	Ceulemans et al., "Functional Diversity of Protein Phosphatase-1, a Cellular Economizer and Reset Button," 2004, Physiol. Rev., 84:1-39
C34†	CHAN et al., "Folate Deprivation Increases Tau Phosphorylation by Homocysteine-induced Calcium Influx and by Inhibition of Phosphatase Activity: Alleviation by S-adenosyl Methionine," 2008, Brain Research, 1199:133-137, ISSN: 0006-8993
C36†	Chao et al., "Structure and Mechanism of the Phosphotyrosyl Phosphatase Activator," 2006, Molecular Cell, 23(4):535-546
C39†	CHEN et al., "Comparison of Protein Phosphatase Inhibition Activities and Mouse Toxicities of Microcystins," 2006, Toxicon, 47(7):742-746, ISSN: 0041-0101
C40†	CHEN et al., "Improved Synthesis and Characterization of L-histidine Norcantharimide, a Novel Potent Protein Phosphatase 2A Inhibitor," 2008, J. of Chinese Pharmaceutical Sciences, 17(2):134-137, ISSN: 1003-1057
C41†	CHEN et al., "Lithium Inhibits Ceramide- and Etoposide-induced Protein Phosphatase 2A Methylation, Bcl-2 Dephosphorylation, Caspase-2 Activation, and Apoptosis," 2006, Molecular Pharmacology, 70(2):510-517, ISSN: 0026-985X
C42†	CHIANG et al., "S-Adenosylmethionine and methylation," 1996, Faseb J, 10:471-80
C43†	Cho & Xu, "Crystal Structure of a Protein Phosphatase 2A Heterotrimeric Holoenzyme," 2007, Nature, 445:53-57
C44†	CHRISTEN et al., "Inhibition of Alpha Interferon Signaling by Hepatitis B Virus," 2007, J. of Virology, 81(1):159-165, ISSN: 0022-538X
C45†	CLARKE et al., "Folate, Vitamin B12, and Serum Total Homocysteine Levels in Confirmed Alzheimer Disease," 1998, Arch Neurol, 55:1449-1155
C46†	CLARKE et al., "Hyper homocysteinemia: an independent risk factor for vascular disease," 1991, N Engl J Med, 324:1149-1155
C58†	DUVAL et al., "analogues of cytotoxics squamocin using reliable reactions: new insights into the reativity and role of the $\alpha,\beta$ -unsaturated lactone of the annonaceous acetogenins," 2006, Tetrahedron, 62(26):6248-6257
C65†	FOLSTAR et al., "Liquid chromatographic coffee wax analysis," 1977, Colloque Scientifique International sure le Café, 8:121-124
C68†	FOWLER et al., "Inhibition of Fatty Acid Amidohydrolase, the Enzyme Responsible for the Metabolism of the Endocannabinoid Anandamide, by Analogues of Arachidonoyl-serotonin," 2003, J. of Enzyme Inhibition and Medicinal Chemistry, 18(3):225-231
C87†	HAHN et al., "Synthesis of 1-alkylisoquinolines and 1,1'-polymethylenediisoquinolines," 1938, Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen, 71B:2183-91
C88†	HAHN et al., "Synthesis of 3-alkyl-4-carbolines and 3,3'-polymethylenedi-4-carbolines," 1938, Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen, 71B:2175-82
C164†	MANO, M.L., "Silicic acid column chromatography in the separation of components of food fats," 1965, Revista Portuguesa de Farmacia, 15(3):398-401
C165†	MARTIN DE LA VEGA et al., "Cerebral Postischemic Reperfusion-induced Demethylation of the Protein Phosphatase 2A Catalytic Subunit," 2002, Journal of Neuroscience Research, 69(4):540-549, ISSN: 0360-4012.
C181†	MUNCH et al., "A sensitive and seletive method for the quantitative determination of fatty acid tryptamides as shell indicators in cocoa products," 1999, Zeitschrift fuer Lebensmittel-Untersuchung und-Forschung A: Food Research and Technology, 208(1):39-43
C182†	MUNCH et al., "Characterization of the substances in cocoa shell. Possibilities to determine the shell percentage in cocoa products by indicators," 1999, Lebensmittelchemie, 53(6):148
C183†	NAGAO et al., "Monitored aminolysis of 3-acylthiazolidine-2-thione: a new convenient synthesis of amide," 1980, Tetrahedron Letters, 21(9):841-4
C184†	NAGAO et al., "Studies on a new synthesis of the acyclic amide and macrocyclic lactam alkaloids," 1979, Koen Yoshishu-Tennen Yuki Kagobutsu Torankai, 22nd, 554-61
C185†	NAGAO et al., "Utilization of sulfur-containing leavng groups. Part IV. Monitored aminolysis of 3-acyl-1,3-thiazolidine-2-thiones: synthesis of amides and amide alkaloids," 1984, Chemical & Pharmaceutical Bulletin, 32(7):2687-99
C212†	RODER et al., "Microtubule-associated protein tau as a therapeutic target in neurodegenerative disease," 2007, Expert Opinion ther. Targets, 11(4):435-442
C213†	ROSZKOWSKI et al., "Enantioselective synthesis of 1-substituted tetrahydro- $\beta$ -carboline derivatives via asymmetric transfer hydrogenation," 2005, J. of Molecular Catalysis A:

	Chemical, 232(1-2):143-149
C222†	SCIORTINO et al., "Antiviral activity. IX. Higher acyl derivatives of sympathomimetic amines of biological significance," 1968, <i>Bollettino Chimico Farmaceutico</i> , 107(8):506-11
C233†	SOMEI et al., "The chemistry of indoles. 87. Syntheses of 1-hydroxytryptamines and serotonin having fatty acyl or (E)-3-phenylpropenoyl derivatives as a Nb-substituent, and a novel homologation on the 3-substituent of the 1-hydroxytryptamines upon treatment with diazomethane," 1998, <i>Heterocycles</i> 48(6):1117-1120
C247†	SZELAG et al., "Determination of the amount of hull-derived lipids in cocoa oils," 1984, <i>Przemysl Spozywczy</i> 38(9):355-7
C248†	SZELAG et al., "Evaluation of behenic acid tryptamide in cocoa fat on the basis of blue value determinations," 1988, <i>Nahrung</i> , 32(3):285-90
C281†	XIE et al., "Methyl Esterification of C-terminal Leucine Residues in Cytosolic 36-kDa Polypeptides of Bovine Brain," 1993, <i>J. of Biological Chemistry</i> , 268(18):13364-13371
C299†	Urban, 1959, "Physiology of some flavonoids and oxycinnamic acid. II. Annual and diurnal periodicity of formation," <i>Planta</i> , 52:565-82.
C300†	Sciortino, 1969, <i>Bollettino Chimico Farmaceutico</i> , 107(8):506-11
C301†	Acker, 1966, <i>Suesswaren</i> , 15(10):622-24, 626-68
C302†	Szelag, 1984, <i>Przemysl Spozywczy</i> , 38(9):355-57
C303†	Nagao, <i>Chemical and Pharmaceutical Bulletin</i> , 32(7):2687-99
C304†	Sacher, 1965, <i>Zeitschrift fuer Lebensmittel-Untersuchung und-Forschung</i> , 128(5):264-67
C305†	Mano, 1965, <i>Revista Portuguesa de Farmacia</i> , 15(3):398-401
C306†	Martin, 1964, <i>Medicamenta</i> , 32(16):9-12
C307†	Hahn, 1938, <i>Berichte der Deutschen Chemischen Gesellschaft</i> , 71B 2175-82, 2183-91

Applicant respectfully submits that no fees are due. If, however, the USPTO disagrees, please charge *only* fees that are *necessary* to maintain pendency and/or protect the filing date of the present application to our Deposit Account Number 03-1721, referencing Attorney's Docket Number 2008725-0051. To the extent that there are any discrepancies between what Applicant has paid with the filing of the present Application and what the USPTO believes is owed, Applicant respectfully requests that a Notice be issued explaining any such discrepancy.

Respectfully submitted,

/Katherine Nicole Clouse/  
Katherine Nicole Clouse, PhD  
Registration Number: 62,750

Choate, Hall & Stewart LLP  
Two International Place  
Boston, MA 02110  
t (617) 248-4903  
f (617) 502-5002  
nclouse@choate.com  
Date: May 28, 2010